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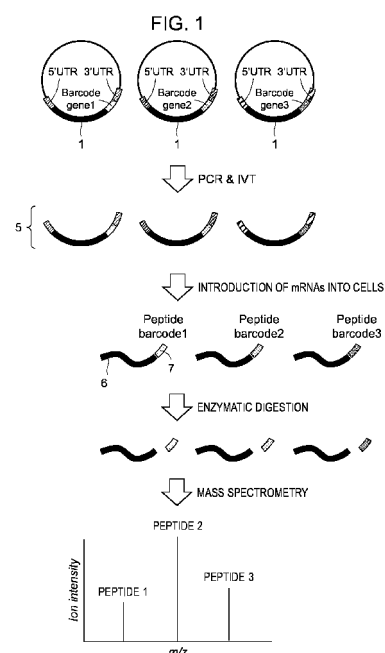
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(54) **METHOD FOR OPTIMIZING MRNA SEQUENCE USING PEPTIDE BARCODE**

(57) There is provided a method for optimizing a nucleic acid sequence, including the steps of: preparing a nucleic acid sequence that includes a candidate sequence containing a sequence of an untranslated region and a sequence encoding a target protein, and a sequence encoding a peptide barcode directly or indirectly linked to the target protein; expressing a protein from the nucleic acid sequence; separating the peptide barcode from the protein; analyzing the separated peptide barcode; and acquiring a relationship between expression of the target protein and the candidate sequence based on a result of the analysis, and selecting an optimal candidate sequence.



(52) Cooperative Patent Classification (CPC): (Cont.)

C-Sets

C12N 15/1065, C12Q 2563/179



EUROPEAN SEARCH REPORT

Application Number

EP 24 19 5540

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	Odunze Uchechukwu ET AL: "A Peptide Barcode Based Approach for Efficient in vivo Screening of RNA Delivery Systems", Research Square, 11 January 2023 (2023-01-11), pages 1-25, XP093237993, DOI: 10.21203/rs.3.rs-2386865/v1 Retrieved from the Internet: URL:https://www.researchsquare.com/article/rs-2386865/v1 [retrieved on 2025-01-15] * page 3, paragraph 3 - page 4, paragraph 3; figure 2 * * page 16, paragraph 2 * * page 15, paragraph 1 *	1-6, 9-11,13	INV. C12N15/10 C12N15/64 C12N15/67 C40B40/08
X	RHYM LUKE H. ET AL: "Peptide-encoding mRNA barcodes for the high-throughput in vivo screening of libraries of lipid nanoparticles for mRNA delivery", NATURE BIOMEDICAL ENGINEERING, vol. 7, no. 7, 1 May 2023 (2023-05-01), pages 901-910, XP093136875, ISSN: 2157-846X, DOI: 10.1038/s41551-023-01030-4 * page 908, right-hand column, paragraph 1 - page 909, left-hand column, paragraph 4; figure 1 *	1,4-6, 9-11	TECHNICAL FIELDS SEARCHED (IPC) C12N C40B
X	JP 2021 016389 A (UEDA ATSUMI) 15 February 2021 (2021-02-15) * paragraph [0095]; figure 1 *	1,2,4, 9-11,13	
-The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
The Hague		17 January 2025	Salminen, Aaro
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	



EUROPEAN SEARCH REPORT

Application Number

EP 24 19 5540

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	EGLOFF PASCAL ET AL: "Engineered peptide barcodes for in-depth analyses of binding protein libraries", NATURE METHODS, NATURE PUBLISHING GROUP US, NEW YORK, vol. 16, no. 5, 22 April 2019 (2019-04-22), pages 421-428, XP036771256, ISSN: 1548-7091, DOI: 10.1038/s41592-019-0389-8 [retrieved on 2019-04-22] * Supplementary Figure 1; page 421, right-hand column, paragraph 2; figures 1-3 * & Egloff Pascal ET AL: "Engineered Peptide Barcodes for In-Depth Analyses of Binding Protein Ensembles, Supplementary Information", Nature methods, 22 April 2019 (2019-04-22), XP093070960, DOI: 10.1038/s41592-019-0389-8 Retrieved from the Internet: URL:https://static-content.springer.com/esm/art:10.1038/s41592-019-0389-8/MediaObjects/41592_2019_389_MOESM1_ESM.pdf [retrieved on 2023-08-04]	1,2,4-13	
A	SAMPLE PAUL J ET AL: "Human 5' UTR design and variant effect prediction from a massively parallel translation assay", NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP US, NEW YORK, vol. 37, no. 7, 1 July 2019 (2019-07-01), pages 803-809, XP036824672, ISSN: 1087-0156, DOI: 10.1038/s41587-019-0164-5 [retrieved on 2019-07-01] * the whole document *	1-13	TECHNICAL FIELDS SEARCHED (IPC)
-The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
The Hague		17 January 2025	Salminen, Aaro
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons	
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DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim
T	SHUN KUMANO ET AL: "Using peptide barcodes for simultaneous profiling of protein expression from mRNA", RAPID COMMUNICATIONS IN MASS SPECTROMETRY, JOHN WILEY & SONS, GB, vol. 38, no. 18, 7 July 2024 (2024-07-07), page n/a, XP072689462, ISSN: 0951-4198, DOI: 10.1002/RCM.9867 * the whole document *	
		TECHNICAL FIELDS SEARCHED (IPC)
-The present search report has been drawn up for all claims		
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The Hague	17 January 2025	Salminen, Aaro
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document		



Application Number

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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1 - 13

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

**LACK OF UNITY OF INVENTION
SHEET B**

Application Number

EP 24 19 5540

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-13

Methods of optimizing a nucleic acid sequence and related kits

2. claims: 14, 15

Methods of preparing a nucleic acid sequence

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